

**Mapping the future of healthcare: precision medicine in practice**

<sup>1</sup>Richa Wadhawan. Professor, Oral Medicine, Diagnosis & Radiology, PDM Dental College & Research Institute, Bahadurgarh, Haryana

<sup>2</sup>Shubham Kumar, Post Graduate, Orthodontics & Dentofacial Orthopedics, Maharana Pratap College Of Dentistry & Research Centre, Gwalior, Madhya Pradesh

<sup>3</sup>Gaurav Dhir, Post Graduate, Orthodontics & Dentofacial Orthopedics, Maharana Pratap College Of Dentistry & Research Centre, Gwalior, Madhya Pradesh

<sup>4</sup>Himani Lau, Professor and Head, Conservative Dentistry and Endodontics, Institute of Dental Education And Advance Studies, Gwalior, Madhya Pradesh

<sup>5</sup>Javeed Majeed Bhat, Private Practitioner, Wellness Dental Care, Kupwara, Jammu & Kashmir

<sup>6</sup>Shruti Singh, Dental Surgeon, Medibuddy, Bengaluru, Karnataka

<sup>7</sup>Vatsal Bhatt, Dental Surgeon, Smile Dental Clinic, Indore, Madhya Pradesh

<sup>8</sup>Suranjita Bora , Consultant Dental Surgeon, Aditya Multispecialty Hospital, Nagaon, Assam

**Corresponding Author:** Richa Wadhawan. Professor, Oral Medicine, Diagnosis & Radiology, PDM Dental College & Research Institute, Bahadurgarh, Haryana.

**Citation of this Article:** Richa Wadhawan, Shubham Kumar, Gaurav Dhir, Himani Lau, Javeed Majeed Bhat, Shruti Singh, Vatsal Bhatt, Suranjita Bora, “Mapping the future of healthcare: precision medicine in practice”, IJDSIR- July – 2024, Volume –7, Issue - 4, P. No. 01 – 14.

**Copyright:** © 2024, Richa Wadhawan, et al. This is an open access journal and article distributed under the terms of the creative common’s attribution non-commercial License. Which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given, and the new creations are licensed under the identical terms.

**Type of Publication:** Original Research Article

**Conflicts of Interest:** Nil

**Abstract**

Precision dentistry utilizes omics sciences to tailor dental care to individual patient needs. Technologies such as genomics, transcriptomics, proteomics, metabolomics, and epigenomics provide detailed biological data for precise diagnosis and treatment planning. Dentists analyze genetic variations, gene expression profiles, protein biomarkers, metabolite levels, and epigenetic modifications to assess oral disease risks, monitor progression, and develop targeted

therapies. This approach enhances treatment outcomes, minimizes side effects, and improves patient satisfaction. Interdisciplinary collaboration is essential for integrating these technologies, emphasizing ethical considerations and obtaining patient consent. As precision medicine advances in dentistry, it promises customized interventions that enhance oral health and patient well-being. Precision medicine improves disease comprehension and treatment by analyzing DNA, RNA, and protein expression, reducing side effects. It

emphasizes disease prevention and early detection through genetic analysis. Advancing technology and genetic insights will revolutionize disease management. Molecular diagnostics and imaging are transforming orthodontic care by efficiently customizing treatments. Computer technology and biomedicine enable personalized therapy and biomechanical planning, with software, hardware, and 3D imaging enhancing orthodontic brackets, highlighting digital technology's pivotal role in the field.

**Keywords:** Personalized Medicine, Dentistry, Orthodontics, Oral Surgery, Periodontics, Endodontics, Oral Carcinoma

## Introduction

Precision medicine, also known as personalized medicine, customizes healthcare by tailoring medical interventions based on individual characteristics such as genetic makeup, environmental factors, lifestyle choices, and personal preferences. It aims to optimize treatment effectiveness, minimize adverse effects, and enhance patient outcomes by individualizing medical decisions and therapies. This approach differs from traditional medicine, which often employs standardized treatments based on generalized population data. Precision medicine utilizes advanced technologies like genetic testing, molecular profiling, and big data analytics to personalize medical care, thereby advancing disease understanding and treatment.<sup>1</sup> In dentistry, precision medicine transforms oral healthcare by harnessing progress in genetics, molecular biology, and data analytics to personalize treatments for each patient. Precision dentistry integrates genetic, environmental, and lifestyle factors to enhance diagnostic accuracy, optimize treatment outcomes, and personalize preventive strategies. By leveraging individual biological characteristics and health risks, this approach improves

dental treatment efficacy and overall patient well-being.<sup>2</sup>

Similar to precision medicine, which tailors treatments based on genetic, lifestyle, and environmental data, precision dentistry promises to revolutionize dental practice by offering tailored disease prevention, diagnosis, and therapy informed by each patient's unique profile. In dentistry, precision medicine revolutionizes practice across specialties: Orthodontists customize treatments for optimal tooth movement and aesthetics using genetic insights. Periodontists predict periodontal disease susceptibility with genetic testing, adjusting preventive strategies. Oral surgeons enhance surgical outcomes and minimize complications through personalized planning based on genetic information. Endodontists improve root canal therapies with genetic analysis for better microbial targeting. Prosthodontists design precise dental prosthetics using genetic profiles for better fit and function.

Pediatric and public health dentists utilize genetic screening to enhance early detection and tailored interventions.<sup>3</sup> Together, these approaches enhance diagnostic accuracy, treatment effectiveness, and patient-centered care in dentistry and beyond, crucial for advancing cancer therapies and various medical conditions. Challenges include integrating diverse data types securely, optimizing model performance, and addressing bias.<sup>4</sup> Successful Artificial Intelligence implementation relies on robust data security, insightful analytics, and collaborative expertise to enhance human capabilities through augmented intelligence. Leveraging big data offers transformative opportunities by managing complex health factors across diverse data types. Artificial Intelligence and big data analytics are revolutionizing healthcare, benefiting stakeholders such as payers, providers, policymakers, patients, and manufacturers.<sup>5</sup> Artificial Intelligence is also pivotal in

combating global healthcare fraud, waste, and abuse. Precision medicine is advancing through Artificial Intelligence-driven personalized approaches, reshaping healthcare delivery models. Ethical concerns, encompassing security, privacy, and human rights, are crucial when deploying Artificial Intelligence applications across virtual health platforms, clinical decision support systems, and surgical robotics, enhancing diagnostics and image-based detection in healthcare. Augmented intelligence enhances disease diagnosis and customizes treatment plans based on individual characteristics and medical history.<sup>6</sup> Artificial Intelligence streamlines administrative tasks such as managing medical records and scheduling appointments, allowing healthcare providers to focus more on patient care. Integrating Artificial Intelligence improves efficiency and care quality, requiring strong ethical oversight to ensure holistic patient well-being, with final healthcare decisions informed by human expertise. Augmented intelligence enhances provider capabilities, reducing errors while preserving the essential human touch in healthcare.<sup>7</sup>

Addressing bias is crucial for equitable care, with tools like IBM's Artificial Intelligence Fairness 360 detecting and correcting biases in datasets. Socio-environmental factors influence AI performance and clinical efficacy, affecting image quality and patient wait times. Validating AI in clinical settings and integrating user feedback are crucial steps prior to widespread adoption, despite healthcare feedback processes being more time-consuming and costly than consumer product evaluations. High-performing AI systems can benefit from synthetic data generation to mimic real-world distributions or simulated environments.<sup>8</sup> Baowaly et al.'s initial Artificial Intelligence efforts are promising, but further research is essential.<sup>9</sup> Data safety and privacy

are critical as Artificial Intelligence integrates diverse data types like genomics and social behaviours in precision medicine. Trust in Artificial Intelligence-enabled services hinges on secure ecosystems for data storage, management, and sharing, requiring advancements in technology, collaborations, regulations, and business models.<sup>10</sup> Augmented intelligence empowers consumers with real-time risk communication and behaviour change tools, enhancing personalized care through timely interventions. Mobile apps, wearables, and voice assistants drive innovations in Artificial Intelligence precision medicine, optimizing health tasks and reducing healthcare costs.<sup>11</sup> High-throughput technologies have revolutionized genetic research, enabling fast and reliable. Whole Genome Sequencing and Whole Exome Sequencing, enriching omics sciences with insights into mRNA, epigenetics, metabolites, proteins, and the microbiome's health impacts. These applications require interdisciplinary expertise spanning engineering, medicine, physics, robotics, computer science, ethics, and biology, driving the advancement of precision medicine. Precision medicine tailors medical therapies to individual patients by leveraging omics sciences like genomics, transcriptomics, epigenomics, proteomics, and metabolomics to integrate data and develop highly predictive models of biological systems. This approach enables rapid diagnosis, dynamic disease assessment, targeted treatment strategies, and reduces costs, psychological strain, and physical stress.<sup>12</sup>

## Discussion

Personalized surgical approaches in medicine are gaining momentum, moving from standardized treatments to customized strategies that meet individual needs. This trend extends to surgical procedures, where techniques are tailored to fit each patient's unique anatomy, promising better outcomes and fewer

complications. Advanced imaging methods like Magnetic Resonance Imaging and Computed Tomography scans support detailed pre-operative planning, ensuring precise implant placement and optimizing recovery. This evolution is particularly significant in areas such as jaw and pre-prosthetic surgery, improving quality of life through more accurate implant positioning and fitting.<sup>13</sup> Moreover, modern advancements such as robotic-assisted surgery and augmented reality enhance surgical accuracy by offering real-time guidance through complex anatomical structures. These innovations also facilitate remote collaboration, allowing global experts to contribute virtually to surgeries and enhancing collective expertise during critical procedures. Despite its promising potential, widespread adoption of personalized surgical approaches faces challenges. Successful implementation requires substantial investments in training, technology, and infrastructure.<sup>14</sup> Surgeons require specialized training for personalized techniques. Precision dentistry and personalized medicine utilize genomic, proteomic, and metabolomic analyses to predict treatment responses, integrating biotechnology and nanotechnology for tailored treatments. Personalized medicine considers patient preferences in treatment planning, while precision dentistry enhances diagnostic accuracy using genetic, biomarker, and socioeconomic factors. These fields aim to customize healthcare based on individual characteristics, though their application in dentistry is emerging with limited patient awareness.<sup>15</sup> This approach promotes patient empowerment, shared decision-making, and treatment alignment with patient values. Advances in high-throughput technology and biological systems drive interest in personalized medicine, aiming to optimize treatment choices and healthcare costs. Effective implementation requires

consideration of non-biological, biological, and environmental factors in decision-making. Validating each personalized treatment strategy through clinical trials is crucial to demonstrate superiority over guideline-based therapies.<sup>16</sup> Precision and personalized medicine tailors interventions based on individual variability, enhancing diagnosis, providing targeted therapies, and improving patient outcomes. Integrating these approaches into routine clinical practice has the potential to revolutionize healthcare delivery and improve population health, applicable also to dentistry by enhancing patient outcomes and managing healthcare costs effectively through genetic screening and targeted preventive care for oral diseases.<sup>17</sup> Predicting patient reactions to anaesthesia and medications through genetic testing can significantly decrease adverse effects. Customizing treatment plans based on genetic and health data enhances patient adherence and acceptance of therapies. Early genetic screening can also minimize the need for invasive diagnostics by identifying high-risk individuals for conditions such as oral cancer. Despite challenges in integrating genetic testing into regular dental practice and addressing logistical and educational barriers, the potential for long-term cost savings and enhanced patient care justifies these efforts.<sup>18</sup> Personalized dentistry utilizes genetic insights and individual health information to tailor treatments for conditions like tooth loss, dental caries, oral cancer, and malocclusion. By customizing preventive measures and treatments based on genetic testing; it optimizes outcomes while navigating ethical considerations around patient privacy and genetic information use. Personalized medicine in dentistry enhances treatment effectiveness, patient satisfaction, and cost-efficiency despite initial costs

and access challenges. Genetic insights, particularly that affecting interleukin-1 (IL-1) production, significantly impact periodontal disease by influencing inflammation in periodontal tissues and disease progression.<sup>19</sup> IL-1 genotype predicts susceptibility to periodontitis, guiding targeted treatments for high-risk individuals, including variants like those in CDKN2BAS linked to aggressive periodontitis. This genetic understanding improves periodontal disease management, optimizing resource allocation and enhancing treatment outcomes effectively. While non-shared factors primarily influence periodontal disease variability, shared environmental factors, like family experiences and habits, also impact edentulism.<sup>20</sup> Rakic et al.'s study assessed osteoprotegerin and RANKL for diagnosing peri-implant mucositis and peri-implantitis, noting bone resorption markers in peri-implant mucositis.<sup>21</sup> Dental caries, a widespread oral health issue affecting many adults and children globally, is primarily caused by bacteria forming biofilms that metabolize sugars into acids, which then erode tooth enamel and dentin. Contributing factors include diet, fluoride use, oral hygiene, saliva composition, enamel structure, taste preferences, and immune responses. Genetic factors such as mutations in genes like Amel X, KLK4, LYSL2, and AJAP1 play a significant role (40-60%) in susceptibility to caries. Early identification of genetic factors can enhance caries management.<sup>22</sup> Research into oral cancer's pathogenesis requires further investigation. Early detection and robust screening using biomarker-based methods are crucial for improving survival rates.<sup>23</sup> Omics technologies, such as genomics and epigenomics, enable precise diagnosis through biomarkers, facilitating personalized therapies tailored to cancer behaviour. Specific antibodies against cancer antigens in head and neck cancer aid early detection. Prompt identification allows for tailored management

strategies including chemotherapy, radiotherapy, and surgery based on cancer cell sensitivity, rather than a uniform protocol.<sup>24</sup>

In orthodontics, genetics plays an increasing role in understanding malocclusion origins, variations, and preventive measures. Research into oral cancer's pathogenesis requires further investigation. Early detection and robust screening using biomarker-based methods are crucial for improving survival rates. Omics technologies, such as genomics and epigenomics, enable precise diagnosis through biomarkers, facilitating personalized therapies tailored to cancer behaviour. Specific antibodies against cancer antigens in head and neck cancer aid early detection. Prompt identification allows for tailored management strategies including chemotherapy, radiotherapy, and surgery based on cancer cell sensitivity, rather than a uniform protocol.<sup>25</sup>

In orthodontics, genetics plays an increasing role in understanding malocclusion origins, variations, and preventive measures. Class III malocclusion, commonly known as Hapsburg jaw, is a monogenic dominant phenotype linked to specific growth factor genes such as Indian hedgehog homolog, parathyroid-hormone like hormone, insulin-like growth factor-1, and vascular endothelial growth factor. This condition is associated with genetic loci including 1p36, 12q23, and 12q13. Genes like transmembrane protein 1 and GAD1 are implicated in cleft lip and palate, while IRF6, PVRL1, and MSX1 variants are linked to syndromic cases.<sup>26</sup> Personalized orthodontics could leverage individual genomic data to anticipate risk factors and deliver precise care for conditions such as cleft lip and palate and Class III malocclusions. Recent advancements in medicine emphasize a shift towards personalized and precise healthcare, enhancing effectiveness and safety by integrating genomic evidence into clinical practices.



With electronic health records, supercomputing, big data analytics, and genetic testing, precision and personalized medicine are advancing rapidly. Precision medicine and personalized medicine have transformed healthcare by acknowledging individual genetic and biological uniqueness, tailoring treatments based on genetic makeup, environmental factors, and lifestyle.<sup>27</sup>

Personalized medicine considers holistic patient attributes like preferences and social context, while precision medicine uses data and analytics for targeted treatments. Advancements in medical technology are enhancing efficiency, cutting costs, and enabling early disease detection and personalized treatment plans. By leveraging genotypic and phenotypic insights for both populations and individuals, these innovations can validate treatment necessity and improve diagnostic accuracy of disease variants.<sup>28</sup> Precision and personalized medicine represent a new era in healthcare, utilizing individual genetics and other sources of variability to tailor treatments and prevent illness. Genomics and other "omic" technologies have been pivotal, enabling this shift from generic to customized medical interventions. This transformative approach promises more precise diagnostics, targeted therapies, and improved patient outcomes, gaining traction across scientific disciplines and poised for further significance in the future. Advancements in genetics and genomics are driving healthcare towards tailored, precise treatments that promise better outcomes. This includes improved disease prevention, accurate diagnoses, safer medication prescriptions, and more effective treatments across various health conditions.<sup>29</sup> High-throughput technology and biological system development have sparked significant interest in this field, enhancing our ability to interpret genetic data and understand physiological processes in health and disease. While

personalized medicine aims to reduce healthcare costs and minimize side effects by optimizing medication choices, it may not be universally applicable to all disorders. In decision-making for various illnesses, it is vital to consider non-biological, biological, and environmental factors. It's also crucial to evaluate the efficacy of personalized treatment strategies through clinical trials, comparing them against standard guideline-based therapies. Precision medicine and personalized medicine have transformative potential in healthcare, offering precise diagnoses, targeted therapies, and enhanced patient outcomes by tailoring interventions to individual needs.<sup>30</sup> Integrating these approaches into clinical practice could revolutionize healthcare delivery and improve population health. Precision medicine advocates for personalized healthcare, adapting medical decisions, treatments, and products to individuals rather than a standardized approach. Advancements in computer technology and biomedicine have similarly transformed orthodontics, enabling customized treatments and boosting efficiency. Assessing pertinent orthodontic technologies and biological research remains critical. Advances in computer software, hardware, and 3D imaging will facilitate more personalized therapy and biomechanical planning. The potential to manufacture personalized orthodontic brackets using advanced materials and digital technology shows promise. Precision medicine integrates genomic, lifestyle, and environmental variations to advance illness prevention and treatment. Orthodontics employs technology to adjust tooth position and improve craniofacial orthopaedics, now advancing into precision orthodontics with personalized appliances and considerations of tissue stress distribution.<sup>31</sup> Computational power, 3D imaging, and omics technologies like metabolomics and genomics

enhance treatment precision by understanding tooth movement and craniofacial osteobiology. This paper explores current and future technological and biomedical advancements in precision orthodontics, facilitated by improved communication technologies and online platforms for data access and search capabilities for healthcare professionals, patients, and the public. This fuels the demand for innovative orthodontic approaches, aiming for personalized, efficient, and optimal care.<sup>32</sup> Advanced 3D imaging like Computed Tomography and Magnetic Resonance Imaging, alongside digital models, enhances diagnosis of dental and skeletal relationships. These methods support computer-assisted surgical planning and custom appliance manufacturing, using 3D printing for precise dental and skeletal adjustments. This approach offers several distinct advantages for treatment planning and implementation.

In silico planning integrates projected dental, skeletal, and soft tissue changes to optimize personalized diagnosis, therapy, and biomechanical planning, reducing complications and improving treatment efficiency and outcomes. Surgical procedures performed prior to full dental adjustments can potentially shorten treatment duration by leveraging biological enhancements like the regional acceleratory phenomenon, though predicting final tooth and jaw positions remains challenging.<sup>33</sup> 3D digital treatment simulation facilitates the custom production of surgical splints and stainless steel archwires, enabling precise planning and execution of dental and skeletal movements. This approach has shown significant reductions in treatment times, improved decompensated jaw-tooth movements, and enhanced aesthetics. Several commercial 3D virtual treatment planning programs have been developed, yet biomechanical planning of tooth movements remains evolving. Examples include

Virtual Surgical Planning Technology by 3D Systems, Simplant and Proplan, and InVivo5® by Anatomage, which integrate Computed Tomography /Cone Beam Computed Tomography data, 3D stereophotogrammetry, and intra-oral occlusal scans for comprehensive 3D views. Collaboration among surgeons, orthodontists, and engineers enables replication of dental movements and osteotomies, translating plans into 3D-designed interim and definitive splints. Advanced orthodontic appliances like SMART Retainer® and TheraMon® use microsensors to track patient compliance and improve treatment outcomes. These advancements include monitoring facemask wear duration; refining procedures based on usage data and applied forces. Developments also feature coils for data acquisition and transfer, and calibration equipment for these systems.<sup>34</sup> SmartArch® orthodontic wires, such as those from Smart Alloys, are programmable for optimal forces, potentially leading to more efficient treatment and shorter appointments. In precision biomedicine for orthodontics, ongoing basic research aims to enhance orthodontic tooth movement, reduce treatment durations, improve tooth anchoring, and modify skeletal growth.<sup>35</sup> Bio-rational therapeutic approaches are developing, indirectly regulating biological activities to amplify tooth movement. Methods for controlling tooth movement and craniofacial growth involve manipulating biological, mechanical, and surgical factors, utilizing advanced wires and appliances, physical and mechanical stimulation, surgically facilitated orthodontic therapy inducing regional acceleratory phenomenon, and localized release of bioactive substances. These methods employ specialized brackets, arch wires, and intermittent forces to control tooth movement effectively. Physical and mechanical stimuli such as vibrational forces, Pulsed Electro Magnetic Field, electrical currents, and low-level

lasers (e.g., Accelident®) are utilized in orthodontics. Surgical facilitated orthodontic procedures like surgery first orthodontics, corticotomy, piezocision, and alveoectomy promote tooth movement through the regional acceleratory phenomenon (e.g., Propel Orthodontics).<sup>36</sup> Biologic and pharmacologic approaches involve enzymes, molecule-mimicking drugs, and genome therapy to modify bone turnover. Experimental studies in birds suggest osteoclast modulation using inhibitors like alendronate bisphosphonate and MMP-13 impacting skeletal malocclusions, while recombinant RANKL affects bone growth. The practical application of bio-pharmaceuticals to control normal skeletal growth and development in orthodontic treatment is still several years away due to the lack of a universally recognized strategy for predicting or quantifying skeletal growth.<sup>37</sup> Further research, including animal models and human clinical trials, is needed to elucidate the biomolecular basis of craniofacial growth and potentially pave the way for future applications of bio-pharmaceuticals in regulating craniofacial skeletal growth. Although several bio-pharmaceuticals have been found to accelerate orthodontic tooth movement and modulate facial growth, additional studies are necessary to evaluate and identify the most effective drugs, determine optimal dosages for maximum efficacy with minimal systemic effects, and develop "smart" drug delivery systems using advanced technologies like nanotechnology and microprocessor-controlled release methods. Patient-specific treatments hold promise in orthodontics despite the intricate interplay of genetic and non-genetic factors. One significant concern in orthodontic care is orthodontically induced external apical root resorption.<sup>38</sup> An observational study involving 195 orthodontic patients analyzed nine clinical and treatment variables, along with single nucleotide polymorphisms from five genes,

to identify risk factors for orthodontically induced external apical root resorption using a multiple linear regression model. This study highlights the fact that interactions between genetic and non-genetic factors are dynamic and evolves over time. For this reason, genetic testing cannot prevent this iatrogenic event.<sup>39</sup> Another work dealing with the effect of supplemental vibratory force on biomarkers of bone remodelling during orthodontic tooth movement and the rate of mandibular anterior alignment examines the concentration of selected biomarkers of bone remodelling with salivary multiplex assay before treatment (T0) and at three following time points (T1, T2, T3). No correlation in the changes in salivary biomarkers of bone remodelling and Reverse Midline Asymmetry Analysis is detected with supplemental vibratory force during orthodontic treatment with fixed appliances. Precision medicine has revolutionized the understanding of orofacial clefts, a diverse group of congenital deformities.<sup>40</sup> Seventy percent are nonsyndromic, while others, like Pierre Robin and Van Der Woude syndromes, include additional malformations affecting multiple systems.<sup>41</sup> Since the 1990s, advances in genomic techniques, bioinformatics, and statistical sciences have identified numerous risk genes and loci. For instance, mutations in the IRF6 gene, identified in 2002, are linked to over 350 mutations covering approximately 70% of Van Der Woude syndrome cases.<sup>42</sup> Genome-wide association studies have identified this gene as pivotal, also implicated in nonsyndromic forms. Furthermore, epigenetic methods are investigating another potential disease mechanism: epi-mutations, involving changes in DNA acetylation and methylation. However, further studies are needed to fully comprehend this field.<sup>43</sup> Bartzela et al., in a retrospective study in 2021, sought to investigate transmission patterns by



analyzing a very large sample of patients and their family members. The data collected are not easy to interpret, partly because there are environmental and additional factors to consider, such as race, gender, age of the parents, and mother's exposure to smoking, alcohol, drugs, infections, and other potentially teratogenic agents during the early months of pregnancy. Their study found that bilateral forms of cleft lip-palate are more frequently associated with syndromes or other malformations and affect the male sex more. The female sex, in contrast, is more affected by cleft palate.<sup>44</sup> In a 2022 study by Thaweesapphithak et al., patients with cleidocranial dysplasia, characterized by skeletal anomalies affecting clavicles, teeth, and cranial sutures, were examined clinically and radiographically. Exome and Sanger sequencing identified heterozygous pathogenic RUNX2 variants in all affected individuals, confirming the genetic basis of cleidocranial dysplasia.<sup>45</sup> The study revealed new or unusual phenotypes alongside typical cleidocranial dysplasia features, such as brachymetatarsia of the left fourth ray, normal clavicles, phalangeal malformations, and unaffected primary dentition. This highlights the efficacy of exome sequencing in detecting mutations across diverse ethnic backgrounds in cleidocranial dysplasia patients. The Runt homology domain is crucial for RUNX2 function, as shown by the two p.Arg225 variants.<sup>46</sup> Precision medicine in pain management employs two main strategies: repurposing medications originally developed for other conditions to target specific pain pathways, and customizing medication treatments based on individual genetic profiles. In the United States, where over 100 million people suffer from chronic pain, opioids like tramadol, oxycodone, and codeine are widely used.

Codeine's conversion to morphine depends largely on the cytochrome P450 2D6 (CYP2D6) enzyme, while tramadol metabolizes into O-desmethyltramadol, a potent opioid receptor agonist. Variants of cytochrome P450 enzymes play a crucial role in drug metabolism. Genetic variations in CYP enzyme genes significantly affect enzyme activity, influencing drug metabolism in individuals.<sup>47</sup> Genotyping provides essential insights into drug response, enabling personalized therapy, particularly for medications metabolized by CYP2C9, CYP2C19, and CYP2D6 enzymes. Approximately 5-10% of people are poor metabolizers lacking CYP2D6 enzyme activity, while 2-11% are intermediate metabolizers with reduced activity. poor metabolizers and intermediate metabolizers may struggle to metabolize codeine and tramadol, potentially leading to inadequate pain relief.<sup>48</sup> Tailoring opioid prescriptions based on CYP2D6 status is supported by Smith et al., demonstrating efficacy.<sup>49</sup> Thomas et al. evaluated postoperative pain management by CYP2D6 phenotype, while Cavallari et al. advocate for clinical adoption of CYP2D6 genotyping to customize opioid dosing, improving pain control post-surgery with inhibitors. Integrating pharmacogenetics into orofacial pain and temporomandibular disorders requires substantial effort.<sup>50</sup> Propranolol effectively relieves facial pain and migraines, but variations in the catechol-O-methyltransferase gene can hinder its effectiveness, as shown by Slade et al. in a randomized controlled trial.<sup>51</sup> Their findings unexpectedly demonstrated that the A allele antagonizes propranolol's efficacy, underscoring the necessity for deeper comprehension of catechol-O-methyltransferase in pain management for precise therapies targeting temporomandibular disorders.<sup>52</sup> Nonetheless, challenges persist, and further investigations are essential, given the extensive number

of enzymes involved in drug metabolism, with known clinical implications for only a subset of them. Personalized medicine not only focuses on treatment but also aims to identify individual cancer risk factors through genetic traits, personal and family medical history, and environmental exposures. Human papillomavirus is a well-known risk factor for specific oral and oropharyngeal carcinoma, highlighting the importance of Human papillomavirus vaccination.<sup>53</sup> Other recognized risks include tobacco, drug, and alcohol use. Dentists play a crucial role in identifying and raising awareness about these factors, advocating for mitigation where necessary. Oral tongue squamous cell carcinoma is highly aggressive, prone to metastasis and recurrence, with a low five-year survival rate. Current TNM staging does not fully encompass patient characteristics such as age, sex, and systemic inflammatory response.<sup>54</sup> Wei Lin et al. conducted a study to create a predictive nomogram for post-surgery survival in oral tongue squamous cell carcinoma, emphasizing clinical traits and serologic inflammation markers like lymphocyte-monocyte ratio and Immunoglobulin G levels.<sup>55</sup> Personalized medicine targets individual cancer risk factors through genetic evaluation, personal and family medical histories, and environmental exposures such as Human Papilloma Virus infection, tobacco, drug, and alcohol use. Dentists play a crucial role in identifying and raising awareness about these factors, advocating for preventive measures where necessary. Oral tongue squamous cell carcinoma, is highly aggressive, with high metastasis and recurrence rates and a poor five-year survival rate. Current TNM staging may not fully consider patient age, sex, or systemic inflammatory response.<sup>56</sup>

## Future Prospects

The future prospects of precision medicine in dentistry are promising and poised to revolutionize oral healthcare in several ways. Advances in genetic screening technologies will enable dentists to assess individual genetic predispositions to oral diseases such as periodontal disease and oral cancers, guiding personalized risk assessments and preventive strategies tailored to each patient's genetic profile. Precision medicine will facilitate the development of targeted therapies based on genetic and molecular profiles, leading to more effective treatments with fewer side effects. Genetic markers identified through precision medicine can aid in early detection of oral diseases before symptoms manifest, allowing for timely interventions and preventive measures to halt disease progression or prevent it altogether. Dentists will be able to create personalized treatment plans considering genetic factors, as well as environmental and lifestyle influences, ensuring treatments are aligned with patient preferences and circumstances.<sup>57</sup>

## Conclusion

Further research is essential despite progress. Ethnic diversity gaps in databases for physical traits underscore the need for extensive collaborative efforts to build comprehensive three-dimensional datasets. Understanding pharmacological impacts on skeletal growth and tooth movement, optimizing dosages, and exploring interactions between metagenomic features and drug actions are crucial. Advanced drug delivery methods like timed-release and localized administration are also critical. Orthodontics can enhance precision by integrating digital technologies, image analysis, and techniques for personalized orthodontic therapies based on patients' molecular genomic profiles.

## References

1. Topol EJ. High-performance medicine: the convergence of human and artificial intelligence. *Nat. Med.* 2019; 25: 44–56.
2. Hashimoto DA et al. Artificial intelligence in surgery: promises and perils. *Ann. Surg.* 2018; 268: 70–76.
3. Nayak S, Patil WAB, Doshi UH. The relationship between salivary insulin-like growth factor I and quantitative cervical maturational stages of skeletal maturity. *J. Orthod.* 2014; 41: 170–174.
4. Wang F & Preininger A. AI in health: state of the art, challenges, and future directions. *Yearb. Med. Inform.* 2019; 28: 16–26.
5. McGinnis JM et al. The case for more active policy attention to health promotion. *Health Aff. (Millwood)*. 2002; 21: 78–93.
6. Joudaki H et al. Improving fraud and abuse detection in general physician claims: a data mining study. *Int. J. Health Policy. Manag.* 2015; 5: 165–172.
7. Davenport T & Kalakota R. The potential for artificial intelligence in healthcare. *Future Healthc. J.* 2019; 6: 94–98.
8. Lander ES. Initial impact of the sequencing of the human genome. *Nature*. 2011; 470: 187–197.
9. Collins FS, Green ED, Guttmacher AE, Guyer MS. On behalf of the US National Human Genome Research Institute. A vision for the future of genomics research. *Nature*. 2003; 422: 835–847.
10. Ginsburg G. Medical genomics: Gather and use genetic data in health care. *Nature*. 2014; 508: 451–453.
11. Dietz HC. New Therapeutic Approaches to Mendelian Disorders. *N. Engl. J. Med.* 2010; 363: 852–863.
12. Petrosino, J.F. The microbiome in precision medicine: The way forward. *Genome Med.* 2018; 10: 12.
13. Ferlay J, Colombet M, Soerjomataram I, Mathers C, Parkin DM, Piñeros M, Znaor A, Bray F. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. *Int. J. Cancer*. 2019; 144: 1941–1953.
14. Mucci, L.A.; Björkman, L.; Douglass, C.W.; Pedersen, N.L. Environmental and Heritable Factors in the Etiology of Oral Diseases—A Population-based Study of Swedish Twins. *J. Dent. Res.* 2005; 84: 800–805.
15. D'silva N, Gutkind JS. Oral Cancer: Integration of Studies for Diagnostic and Therapeutic Precision. *Adv. Dent. Res.* 2019; 30: 45–49.
16. Brandwein-Gensler M., Smith RV, Wang B, Penner C, Theilken A, Broughel D, Schiff B, Owen RP, Smith J, Sarta C. et al. Validation of the Histologic Risk Model in a New Cohort of Patients with Head and Neck Squamous Cell Carcinoma. *Am. J. Surg. Pathol.* 2010; 34: 676–688.
17. Schmitd LB, Scanlon CS, D'silva NJ. Perineural Invasion in Head and Neck Cancer. *J. Dent. Res.* 2018; 97: 742–750.
18. Vermorken JB, Mesia R, Rivera F, Remenar E, Kawecki A, Rottey S, Erfan J, Zabolotnyy D, Kienzer H.R, Cupissol D. et al. Platinum-Based Chemotherapy plus Cetuximab in Head and Neck Cancer. *N. Engl. J. Med.* 2008; 359: 1116–1127.
19. Hemadi AS, Huang R, Zhou Y, Zou J. Salivary proteins and microbiota as biomarkers for early childhood caries risk assessment. *Int. J. Oral Sci.* 2017; 9: e1.
20. Inchingolo F, DiPalma G, Cirulli N, Cantore S, Saini RS., Altini V, Santacroce L, Ballini A, Saini R.

- Microbiological results of improvement in periodontal condition by administration of oral probiotics. *J. Biol. Regul. Homeost. Agents.* 2018; 32:1323–1328.
21. Bonner JA, Harari PM., Giralt J, Azarnia N, Shin DM., Cohen RB, Jones CU, Sur R, Raben D, Jassem J et al. Radiotherapy plus Cetuximab for Squamous-Cell Carcinoma of the Head and Neck. *N. Engl. J. Med.* 2006; 354: 567–578.
  22. Ballini A, Cantore S, Saini R, Pettini F, Fotopoulou EA, Saini SR, Georgakopoulos IP, DiPalma G, Isacco CG, Inchingolo F. Effect of activated charcoal probiotic toothpaste containing *Lactobacillus paracasei* and xylitol on dental caries: A randomized and controlled clinical trial. *J. Biol. Regul. Homeost. Agents.* 2019, 33, 977–981.
  23. Di Naro E, Loverro M, Converti I, Loverro MT, Ferrara E, Rapone B. The Effect of Menopause Hypoestrogenism on Osteogenic Differentiation of Periodontal Ligament Cells (PDL) and Stem Cells (PDLs): A Systematic Review. *Healthcare.* 2021; 9:572.
  24. Ballini A, Cantore S, Farronato D, Cirulli N, Inchingolo F, Papa F, Malcangi G, Inchingolo AD, DiPalma G, Sardaro N et al. Periodontal disease and bone pathogenesis: The crosstalk between cytokines and *porphyromonas gingivalis*. *J. Biol. Regul. Homeost. Agents.* 2015; 29: 273–281.
  25. Czerninski R, Amornphimoltham P, Patel V, Molinolo AA, Gutkind JS. Targeting Mammalian Target of Rapamycin by Rapamycin Prevents Tumor Progression in an Oral-Specific Chemical Carcinogenesis Model. *Cancer Prev. Res.* 2009; 2:27–36.
  26. Li X, Feng L, Zhang C, Wang J, Wang S, Hu L. Insulin-like growth factor binding proteins 7 prevents dental pulp-derived mesenchymal stem cell senescence via metabolic downregulation of p21. *Sci. China Life Sci.* 2022; 65:2218–2232.
  27. Chow LQM, Haddad R., Gupta S, Mahipal A, Mehra R, Tahara M, Berger R., Eder JP, Burtness, B, Lee SH. et al. Antitumor Activity of Pembrolizumab in Biomarker-Unselected Patients with Recurrent and/or Metastatic Head and Neck Squamous Cell Carcinoma: Results from the Phase Ib KEYNOTE-012 Expansion Cohort. *J. Clin. Oncol.* 2016; 34: 3838–3845.
  28. Ballini A, Dipalma G, Isacco CG, Boccellino M., Di Domenico M., Santacroce L, Nguyễn, KC, Scacco S, Calvani M, Boddi A et al. Oral Microbiota and Immune System Crosstalk: A Translational Research. *Biology.* 2020; 9:131.
  29. The Global Alliance for Genomics and Health A federated ecosystem for sharing genomic, clinical data. *Science* 2016, 352:1278–1280.
  30. Ballini A, Santacroce L, Cantore S, Bottalico L, Dipalma G, Topi S, Saini R., De Vito D, Inchingolo F. Probiotics Efficacy on Oxidative Stress Values in Inflammatory Bowel Disease: A Randomized Double-Blinded Placebo-Controlled Pilot Study. *Endocr. Metab. Immune Disord. Drug Targets* 2019; 19:373–381.
  31. Gilbert JA, Quinn RA, Debelius J, Xu ZZ, Morton J, Garg N, Jansson JK, Dorrestein PC, Knight R. Microbiome-wide association studies link dynamic microbial consortia to disease. *Nature.* 2016; 535: 94–103.
  32. Inchingolo AM, Gargiulo Isacco C, Inchingolo AD, Nguyen KCD, Cantore S, Santacroce L, Scacco S, Cirulli N, Corriero A, Puntillo F et al. The Human Microbiota Key Role in the Bone Metabolism

- Activity. *Eur. Rev. Med. Pharmacol. Sci.* 2023; 27: 2659–2670.
33. Belibasakis GN, Bostanci N, Marsh PD, Zaura E. Applications of the oral microbiome in personalized dentistry. *Arch. Oral Biol.* 2019; 104: 7–12.
34. Acharya A, Chan Y, Kheur S, Jin LJ, Watt RM, Mattheos N. Salivary microbiome in non-oral disease: A summary of evidence and commentary. *Arch. Oral Biol.* 2017; 83: 169–173.
35. Cantore S, Ballini A, De Vito D, Abbinante A, Altini V, DiPalma G, Inchingolo F, Saini R. Clinical results of improvement in periodontal condition by administration of oral probiotics. *J. Biol. Regul. Homeost. Agents.* 2018; 32: 1329–1334.
36. Dipalma G, Inchingolo AD, Inchingolo F, Charitos IA, Cosola MD, Cazzolla AP. Focus on the cariogenic process: Microbial and biochemical interactions with teeth and oral environment. *J. Biol. Regul. Homeost. Agents.* 2021; 35: 429–440.
37. Inchingolo F, Santacroce L, Cantore S, Ballini A, Del Prete R, Topi S, Saini R, Dipalma, G, Arrigoni R. Probiotics and EpiCor® in human health. *J. Biol. Regul. Homeost. Agents.* 2019; 33: 1973–1979.
38. Silva HC, Lavado N, Canova F, Lopez MG, Regateiro FJ, Pereira SA. Influence of clinical factors on the protective or deleterious impact of genetic variants in orthodontically induced external root resorption: An observational study. *BMC Oral Health.* 2022; 22: 270.
39. Inchingolo F, Martelli FS, Gargiulo Isacco C, Borsani E, Cantore S, Corcioli F, Boddi A, Nguyễn KCD, De Vito D, Aityan SK et al. Chronic Periodontitis and Immunity, Towards the Implementation of a Personalized Medicine: A Translational Research on Gene Single Nucleotide Polymorphisms (SNPs) Linked to Chronic Oral Dysbiosis in 96 Caucasian Patients. *Biomedicines.* 2020; 8:115.
40. Beck JD, Philips K, Moss K, Divaris K., Morelli T, Offenbacher S. Advances in precision oral health. *Periodontol.* 2000. 2020; 82:268–285.
41. Cuevas-Córdoba B, Santiago-Garcia J. Saliva: A Fluid of Study for OMICS. *OMICS.* 2014; 18:87–97.
42. Lin X, Zhou W, Liu Z, Cao W, Lin C. Targeting cellular metabolism in head and neck cancer precision medicine era: A promising strategy to overcome therapy resistance. *Oral Dis.* 2022; 00: 1–20.
43. Contaldo M, Fusco A, Stiuso P, Lama S, Gravina AG, Itro A, Federico A, Itro A, Dipalma G Inchingolo F et al. Oral Microbiota and Salivary Levels of Oral Pathogens in Gastro-Intestinal Diseases: Current Knowledge and Exploratory Study. *Microorganisms.* 2021; 9:1064.
44. Fine DH, Markowitz K, Furgang D, Fairlie K, Ferrandiz J, Nasri C, McKiernan M., Donnelly R, Gunsolley J. Macrophage Inflammatory Protein-1α: A Salivary Biomarker of Bone Loss in a Longitudinal Cohort Study of Children at Risk for Aggressive Periodontal Disease? *J. Periodontol.* 2009; 80: 106–113.
45. Thaweesapphithak, S.; Saengsin, J.; Kamolvisit, W.; Theerapanon, T.; Porntaveetus, T.; Shotelersuk, V. Cleidocranial dysplasia and novel RUNX2 variants: Dental, craniofacial, and osseous manifestations. *J. Appl. Oral Sci.* 2022;30:e20220028.
46. Inchingolo AD, Malcangi G, Semjonova A, Inchingolo AM, Patano A, Coloccia G, Ceci S, Marinelli G, Di Pede, C.; Ciocia, A.M.; et al. Oralbiotica/Oralbiotics: The Impact of Oral Microbiota on Dental Health and Demineralization:



- A Systematic Review of the Literature. *Children*. 2022; 9:1014.
47. Molinolo AA, Hewitt SM, Amornphimoltham P, Keelawat S, Rangdaeng S, García AM, Raimondi AR, Jufe R, Itoiz M, Gao Y et al. Dissecting the Akt/Mammalian Target of Rapamycin Signaling Network: Emerging Results from the Head and Neck Cancer Tissue Array Initiative. *Clin. Cancer Res*. 2007; 13: 4964–4973.
48. Ebersole JL, Nagarajan R, Akers D, Miller CS. Targeted salivary biomarkers for discrimination of periodontal health and disease(s). *Front. Cell. Infect. Microbiol*. 2015; 5: 62.
49. Mayo RC & Leung J. Artificial intelligence and deep learning - radiology's next frontier? *Clin. Imaging*. 2018; 49: 87–88.
50. Inchingolo F, Ballini A, Georgakopoulos PG, Inchingolo AD, Tsantis S, Vito DD, Cantore S, Georgakopoulos IP, Dipalma G. Immediate implant placement by using bone-albumin allograft and concentrated growth factors (cgfs): Preliminary results of a pilot study. *Oral Implantol*. 2018; 11: 31–40.
51. Inchingolo F, Ballini A, Cagiano R., Inchingolo AD, Serafini M, De Benedittis M, Cortelazzi R, Tatullo M, Marrelli M., Inchingolo AM et al. Immediately loaded dental implants bioactivated with platelet-rich plasma (PRP) placed in maxillary and mandibular region. *Clin. Ter*. 2015; 166: e146–e152.
52. Inchingolo F, Ballini A, Mura SA, Farronato D, Cirulli N, Pettini F, Gheno E, Vermesan D, Pederzoli P, Resta G et al. Use of platelet rich fibrin and Bio-OSS/SINT-Oss for implant-prosthetic rehabilitation in maxillary atrophy with sinus pathology: A 48-month follow-up. *Eur. J. Inflamm*. 2015; 13:58–65.
53. Lyford-Pik S, Peng S, Young GD, Taube JM., Westra WH, Akpeng B, Bruno TC, Richmon JD, Wang H, Bishop JA. et al. Evidence for a Role of the PD-1:PD-L1 Pathway in Immune Resistance of HPV-Associated Head and Neck Squamous Cell Carcinoma. *Cancer Res*. 2013; 73:1733–1741.
54. Cantore S, Ballini A, De Vito D, Martelli FS, Georgakopoulos I, Almasri M, Dibello V, Altini V, Farronato G, DiPalma G et al. Characterization of human apical papilla-derived stem cells. *J. Biol. Regul. Homeost. Agents*. 2017; 31:901–910.
55. Casu C, Mosaico G, Natoli V, Scarano A, Lorusso F, Inchingolo F. Microbiota of the Tongue and Systemic Connections: The Examination of the Tongue as an Integrated Approach in Oral Medicine. *Hygiene*. 2021; 1: 56–68.
56. Lin YW, Kang WP, Huang BL, Qiu ZH, Wei LF, Zhang B, Ding TY, Luo Y, Liu CT, Chu LY et al. Nomogram based on clinical characteristics and serological inflammation markers to predict overall survival of oral tongue squamous cell carcinoma patient after surgery. *BMC Oral Health*. 2021; 21:667.
57. Rapone B, Ferrara E, Santacroce L, Topi S, Gnoni A, Dipalma G, Mancini A, Di Domenico M, Tartaglia GM, Scarano A et al. The Gaseous Ozone Therapy as a Promising Antiseptic Adjuvant of Periodontal Treatment: A Randomized Controlled Clinical Trial. *Int. J. Environ. Res. Public Health*. 2022; 19:985.